## REMARKS

Claims 1-50 are pending in the application. For reasons detailed below, the rejections should be withdrawn and the claims allowed to issue. Entry of the foregoing amendments is respectfully requested.

1. The Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-50 are rejected under 35 U.S.C. §112, second paragraph. The Examiner alleges that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claims 1-50 are indefinite for reciting "said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions" in claims 1, 30, 34, and 38 because the exact meaning of the phrase is not clear. In addition claims 33, 36 and 37 recite "a substrate for the enzyme" and there is insufficient antecedent basis for this limitation in the claim.

In response to the rejections of the Examiner, Applicants have (i) amended subsection (a) of claims 1, 30, 34 and 38 to recite "said antigen is free of HLA-antigen and substantially free of non-immunogenic glycoproteins" and (ii) claims 33, 36 and 37 have been amended to correct the antecedent basis.

2. The Rejections Under 35 U.S.C. §112, First Paragraph

Claims 2-6, 17-29, 34-35, 38-41, 43, 47 and 49-50 are rejected under 35 U.S.C.§112, first paragraph. According to the Examiner, the specification does not

provide evidence that the claimed biological materials are (i) known and readily available to the public and (ii)reproducible from the written description.

Hybridoma cell lines 33.28, Chi#1, and 31.1 have been deposited with the American Type Culture Collection under the provisions of the Budapest Treaty. All restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application.

Additionally, as set forth in the attached Verified Statement of Dr. Myron Arlen, inventor of the above identified invention, the biological material described in the specification as filed is the same as that deposited in the ATTC. Furthermore, the deposited material was in Applicant's possession at the time the application was filed.

The Examiner alleges that the claims recite an antibody specific for a purified human colon carcinoma-associated protein antigen that is (i) characterized by a purification method; (ii) not detected in normal cells or in cells other than colon carcinoma; (iii) immunogenic; and (iv) induces an immune response. According to the Examiner, the specification only teaches a 61.1 kD and 72 kD protein with the claimed characteristics, however, the claims are broadly drawn to any molecular weight protein with the claimed characteristics. Thus, it would be reasonable to for one of skill in the art to conclude that the inventors were not in possession of the invention at the time the application was filed.

Applicants respectfully disagree with the Examiner. Applicants' pending claims encompass monoclonal antibodies that bind to an antigen with four different identifying characteristics, *i.e.*, (i) characterization by a purification method; (ii) absence in normal cells or in cells other than colon carcinoma; (iii) immunogenicity; and (iv) ability to

induce an immune response. In addition, as set forth in the specification, Applicants clearly demonstrated the production of monoclonal antibodies that bind to an antigen with each of these unique characteristics. Thus, one skilled in the art would conclude that the inventors were indeed in possession of the invention at the time the application was filed.

3. The Claims Are Not Anticipated

Claim 1, 8-9 are rejected under 35 U.S.C.§102(b) as being anticipated by Herlyn et al (PNAS 76:1138, 3/79;"Herlyn"). According to the Examiner, the claims recite an antibody specific for an antigen characterized by a purification and wherein the antigen is not detected on human carcinoma cells other than colon and is not detected on normal tissue and the antigen is immunogenic in human and induces an immune response and is radiolabeled.

The Examiner alleges that Herlyn teaches antibodies to antigens from colon carcinoma cells and the antibody does not bind to normal cells and the antibody is radiolabled. In addition, it would be inherent that the antigen would induce an immune response in humans because the antigen is not found in normal tissue. Thus the art reads on the claims.

Applicants assert that Herlyn fails to anticipate the claimed antibody molecules Herlyn's antibodies possess properties that differ from those of Applicants. One such property is the ability of Applicants' antibodies to stimulate an immune response in humans which is expressed as cell mediated immunity. Such immunity, referred to as antibody-dependent cellular cytotoxicity (ADCC) is associated with destruction of

tumors. Herlyn fails to disclose antibody molecules capable of such cell-mediated immunity. Further, Herlyn discloses that the 1083-17 and 1116-56 antibodies fail to bind to the colorectal carcinoma cell line SW480 (see, p.1439, column 2, first full paragraph). This is in contrast to Applicants' antibody molecules which clearly bind to SW480 cells (see, Table 4 of the specification).

Claims 1, 8 are rejected under 35 U.S.C.§102(b) as being anticipated by Hollinshead et al. (Cancer 56:480-489, 1985; "Hollinshead"). The Examiner maintains that Hollinshead teach monoclonal antibody to a colon carcinoma which induces an immune response and the antigen is not present in normal tissue and the antibody is used in an ELISA.

The claims are not anticipated by Hollinshead. First, Hollinshead merely discloses the purification of two colon carcinoma tumor associated antigens (TAA) and the use of those antigens in immunotherapy. Such immunotherapy involves the immunization of a subject with the purified TAAs for stimulation of a cell mediated immune response. Second, although Hollinstead ***mentions*** characterization of monoclonal antibodies against TAA, such characterizations are absent from the cited Hollinshead reference. Indeed, Hollinstead refers to the publication of such characterizations as "in preparation" (see reference 11 of Hollinstead).

Claim 1 is rejected under 35 U.S.C.§102(b) as being anticipated by Price et al (IRCS Journal of Medical Science 13:366-367, 1985;"Price"). The Examiner alleges that Price teaches an antibody to a colon carcinoma antigen wherein the antigen is in colon carcinoma cells and not in normal colon cells.

Applicants maintain that Price describes the production of a monoclonal antibody that is immunospecific for the ***anti-carcinoembryonic antigen*** (CEA). In contrast, Applicants have generated monoclonal antibodies against proteins other than that of CEA. In this regard, the Examiner's attention is directed to column 21, lines 63-66, of the specification which indicates that the purified colon carcinoma antigens utilized by Applicants to generate the claimed monoclonal antibodies were ***"distinct from that of carcinoembryonic antigen."***

Thus, given the differences between the disclosures of Herlyn, Hollinshead and Price and the subject matter encompassed by the pending claims, the claims cannot be anticipated.

4. The Claimed Invention is Not Obvious

Claim 1, 7-15, 30-33, 36-37, 42, 44, 45, 48 are rejected under 35 U.S.C.§103(a) as being unpatentable over Hollinshead as applied to claims 1 and 8 above, and further in view of Neuberger et al (WO 86/01533, published 3/86;"Neuberger").

The Examiner maintains that although Hollinshead does not teach a chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody, these deficiencies are made up for in the teaching of Neuberger. Neuberger is alleged to teach chimeric antibodies and antibodies that can be labeled with toxins, radiolables, dyes, cytotoxic agents and that the antibody can be immobilized for affinity chromatography. Therefore, according to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art at the time the

claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Hollinshead and Neuberger.

Claims 1, 7-15, 30-33, 36-37, 42, 45, and 48 are rejected under 35 U.S.C.§103(a) as being unpatentable over Herlyn or Price and further in view of Neuberger.

The Examiner alleges that although Herlyn and Price do not teach chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger. Neuberger is alleged to teach chimeric antibodies and antibodies that can be labeled with toxins, rabiolables, dyes, cytotoxic agents and the antibody can be immobilized for affinity chromatography.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Herlyn or Price in view of Neuberger et al.

As indicated above, each of the Herlyn, Hollingshead or Price references fails to disclose monoclonal antibodies having the limitations set forth in the pending claims. The Neuberger reference fails to provide, or even suggest, the deficiencies found in the teachings of Herlyn, Hollingshead or Price. Thus, the claimed invention cannot be rendered obvious in view of the cited references.

## CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by the amended claims is patentable over the rejections of the Examiner. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

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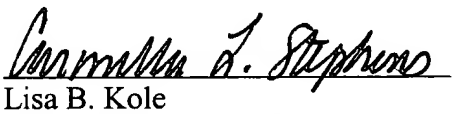

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